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# Cancer of Unknown Primary Causes, Risk Factors, and Prevention

## Risk Factors

Since the exact type of cancer is not known, it's hard to identify factors that might affect risk. But research has provided some information about possible risk factors for these cancers.

- [Cancer of Unknown Primary Risk Factors](#)
- [What Causes a Cancer of Unknown Primary?](#)

## Prevention

Even though the origin of this cancer is unclear, certain lifestyle changes may help to reduce your risk.

- [Can a Cancer of Unknown Primary Be Prevented?](#)

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# Cancer of Unknown Primary Risk Factors

A risk factor is anything that affects a person's chance of getting a disease such as cancer. Different cancers have different risk factors. Some risk factors, like smoking,

can be changed. Others, like a person's age or family history, can't be changed.

But having a risk factor, or even several, does not mean that a person will get the disease, and many people get cancer without having any known risk factors.

Since the exact type of cancer is not known, it's hard to identify factors that might affect risk for cancer of unknown primary (CUP). These cancers are also a very diverse group, making this issue even more complicated. But there is research that provides some information about CUP risk factors.

[Smoking](#)<sup>1</sup> is probably an important risk factor for CUP. More than half of patients with CUP have a history of smoking. When autopsy studies are done, many cancers of unknown primary are found to have started in the pancreas, lungs, kidneys, throat, larynx, or esophagus. Smoking increases the risk for all of these cancers.

Some other cancers of unknown primary are eventually found to have started in the stomach, colon, rectum, or ovaries. [Diet, nutrition](#)<sup>2</sup>, and [weight](#)<sup>3</sup> are factors that have been linked to these cancers. For more information, see the specific [type of cancer](#)<sup>4</sup>.

Melanoma (an aggressive type of [skin cancer](#)<sup>5</sup>) is another source of cancer of unknown primary. An important melanoma risk factor is exposure to [ultraviolet radiation](#)<sup>6</sup> in sunlight.

Overall, however, there are no factors that specifically increase the risk of cancer of unknown primary. Even in people who may have one or more of the risk factors above, it's not possible to know for sure if these factors contributed to the cancer.

## Hyperlinks

1. [www.cancer.org/cancer/cancer-causes/tobacco-and-cancer.html](http://www.cancer.org/cancer/cancer-causes/tobacco-and-cancer.html)
2. [www.cancer.org/cancer/cancer-causes/diet-physical-activity.html](http://www.cancer.org/cancer/cancer-causes/diet-physical-activity.html)
3. [www.cancer.org/cancer/cancer-causes/diet-physical-activity/body-weight-and-cancer-risk.html](http://www.cancer.org/cancer/cancer-causes/diet-physical-activity/body-weight-and-cancer-risk.html)
4. [www.cancer.org/cancer.html](http://www.cancer.org/cancer.html)
5. [www.cancer.org/cancer/skin-cancer.html](http://www.cancer.org/cancer/skin-cancer.html)
6. [www.cancer.org/cancer/cancer-causes/radiation-exposure/uv-radiation.html](http://www.cancer.org/cancer/cancer-causes/radiation-exposure/uv-radiation.html)

## References

Greco FA, Hainsworth JD. Carcinoma of Unknown Primary In: DeVita VT, Lawrence TS,

Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 10<sup>th</sup> ed. Philadelphia, PA: Lippincott Williams & Wilkins 2015: 1719-1736.

Hemminki K, Chen B, Melander O, Manjer J, Hallmans G, Hemminki A. Smoking and body mass index as risk factors for subtypes of cancer of unknown primary. *Int J Cancer*. 2015 Jan 1;136(1):246-7. doi: 10.1002/ijc.28969.

Löffler H, Puthenparambil J, Hielscher T, Neben K, Krämer A. Patients with cancer of unknown primary: A retrospective analysis of 223 patients with adenocarcinoma or undifferentiated carcinoma. *Dtsch Arztebl Int*. 2014 Jul 7;111(27-28):481-7. doi: 10.3238/arztebl.2014.0481.

Varadhachary GR, Lenzi R, Raber MN, Abbruzzese JL. Carcinoma of Unknown Primary In: Neiderhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5<sup>th</sup> ed. Philadelphia, PA. Elsevier: 2014:1792-1803.

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## What Causes a Cancer of Unknown Primary?

Cancers of unknown primary (CUP) include a variety of cancers, which may each have a number of different causes. This is why it's hard to assign a particular cause to CUP.

Cancer is the result of changes in a cell's DNA. In recent years, scientists have made great progress in learning how certain changes in DNA can cause normal cells to become cancerous. DNA is the chemical in each of our cells that makes up our genes, which control how our cells function. We usually look like our parents because they are the source of our DNA. But DNA affects more than how we look.

Some genes control when our cells grow and divide into new cells:

- Certain genes that help cells grow and divide are called **oncogenes**.
- Genes that help keep cell division under control or cause cells to die at the right time are called **tumor suppressor genes**.

Cancers can be caused by DNA changes that turn on oncogenes or turn off tumor suppressor genes.

Most of the DNA changes related to CUP probably occur during a person's lifetime rather than having been inherited before birth. These are called **acquired** or **sporadic** mutations. These kinds of mutations may sometimes result from known exposures such as tobacco smoke, ultraviolet light, radiation, or certain cancer-causing chemicals, but often they occur for no apparent reason.

As scientists learn more about how cancers develop, they are also beginning to understand why some cancers tend to grow and spread so quickly that they are diagnosed as cancers of unknown primary.

## References

Greco FA, Hainsworth JD. Carcinoma of Unknown Primary In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 10<sup>th</sup> ed. Philadelphia, PA: Lippincott Williams & Wilkins 2015: 1719-1736.

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# Can a Cancer of Unknown Primary Be Prevented?

Cancer of unknown primary (CUP) represents a number of different cancers, so there is no known way to prevent it. Still, certain lifestyle changes may reduce the risk of many types of cancer. This might in turn reduce a person's risk of CUP.

Smoking is one of the most significant [risk factors](#) that a person can control, and is thought to be directly related to deaths from cancer. Quitting or never starting reduces

the risk of cancers of many types, including those of unknown primary. Please call us if you need help quitting tobacco. This, and a lot more [information about tobacco](#)<sup>1</sup>, can be read online or mailed to you.

Factors linked with [body weight](#)<sup>2</sup>, [physical activity, and eating patterns](#)<sup>3</sup> are also known to affect the risk for different types of cancers and deaths related to cancer. Staying at a [healthy weight](#)<sup>4</sup> throughout life, being [physically active](#)<sup>5</sup>, following a [healthy eating pattern](#)<sup>6</sup>, and limiting [alcohol intake](#)<sup>7</sup> can all help reduce your risk of cancer.

Because the exact type and the origin of a CUP are unknown, it's not possible to say how any particular case might have been prevented. It is important to realize that many people with cancer have no apparent risk factors, and there's nothing they could have done to avoid the disease.

## Hyperlinks

1. [www.cancer.org/cancer/cancer-causes/tobacco-and-cancer.html](http://www.cancer.org/cancer/cancer-causes/tobacco-and-cancer.html)
2. [www.cancer.org/cancer/cancer-causes/diet-physical-activity/body-weight-and-cancer-risk.html](http://www.cancer.org/cancer/cancer-causes/diet-physical-activity/body-weight-and-cancer-risk.html)
3. [www.cancer.org/healthy/eat-healthy-get-active.html](http://www.cancer.org/healthy/eat-healthy-get-active.html)
4. [www.cancer.org/healthy/eat-healthy-get-active/take-control-your-weight.html](http://www.cancer.org/healthy/eat-healthy-get-active/take-control-your-weight.html)
5. [www.cancer.org/healthy/eat-healthy-get-active/get-active.html](http://www.cancer.org/healthy/eat-healthy-get-active/get-active.html)
6. [www.cancer.org/healthy/eat-healthy-get-active/eat-healthy.html](http://www.cancer.org/healthy/eat-healthy-get-active/eat-healthy.html)
7. [www.cancer.org/cancer/cancer-causes/diet-physical-activity/alcohol-use-and-cancer.html](http://www.cancer.org/cancer/cancer-causes/diet-physical-activity/alcohol-use-and-cancer.html)

## References

Greco FA, Hainsworth JD. Carcinoma of Unknown Primary In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 10<sup>th</sup> ed. Philadelphia, PA: Lippincott Williams & Wilkins 2015: 1719-1736.

Hemminki K, Chen B, Melander O, Manjer J, Hallmans G, Hemminki A. Smoking and body mass index as risk factors for subtypes of cancer of unknown primary. *Int J Cancer*. 2015 Jan 1;136(1):246-7. doi: 10.1002/ijc.28969.

Rock CL, Thomson C, Gansler T, et al. American Cancer Society guideline for diet and physical activity for cancer prevention. *CA: A Cancer Journal for Clinicians*. 2020;70(4). doi:10.3322/caac.21591. Accessed at

<https://onlinelibrary.wiley.com/doi/full/10.3322/caac.21591> on June 9, 2020.

Søndergaard D, Nielsen S, Pedersen CNS, Besenbacher S. Prediction of primary tumors in cancers of unknown primary. *J Integr Bioinform*. 2017 Jul;14(2):pii. doi: 10.1515/jib-2017-0013.

Varadhachary GR, Lenzi R, Raber MN, Abbruzzese JL. Carcinoma of Unknown Primary In: Neiderhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5<sup>th</sup> ed. Philadelphia, PA. Elsevier: 2014:1792-1803.

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